

12/20/03
Application No.: 09/982,892
Amendment Dated 29 December 2003
Response to Office Action of 27 June 2003

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims

1 (Original): A bioconjugate of a bioactive agent and an organocobalt complex wherein the bioactive agent is covalently conjugated to the cobalt atom ^{of the organocobalt complex} through a non-reactive atom in the bioactive agent molecule, wherein said bioactive agent is selected from the group consisting of a peptide, a peptide analogue, a protein, a protein analogue, a nucleic acid and a nucleic acid analogue.

2 (Original): The bioconjugate of claim 1, wherein said non-reactive atom is selected from the group consisting of a carbon atom, a nitrogen atom, an oxygen atom, a sulfur atom, a selenium atom or a silicon atom.

3 (Original): The bioconjugate of claim 1, wherein said non-reactive atom is a carbon atom.

4 (Original): The bioconjugate of claim 1, wherein the non-reactive carbon atom is a carbon atom from an alkyl, acyl or aryl group that will not lead to rearrangement or destruction of the bioactive agent under conditions of ligand exchange during receptor-mediated endocytosis.

5 (Original): The bioconjugate of claim 1, wherein said bioactive agent is covalently bound directly to the cobalt atom of the organocobalt complex.

6 (Original): The bioconjugate of claim 1, wherein said bioactive agent is covalently bound indirectly to the cobalt atom of the organocobalt complex via a spacer.

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7 (Original): The bioconjugate of claim 6, wherein said spacer is a self-destructing linker.

8 (Original): The bioconjugate of claim 1, wherein said bioactive agent is a peptide or peptide analogue.

9 (Original): The bioconjugate of claim 1, wherein said bioactive agent is a protein or protein analogue.

10 (Original): The bioconjugate of claim 1, wherein said bioactive agent is a nucleic acid or a nucleic acid analogue.

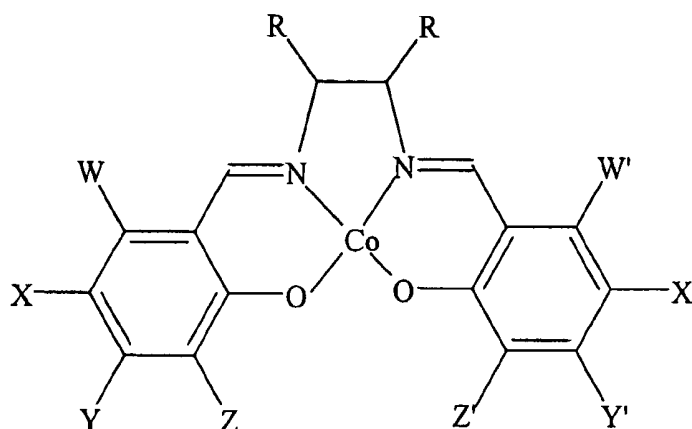
11 (Original): The bioconjugate of claim 10, wherein said nucleic acid or nucleic acid analogue is a polynucleotide.

12 (Original): The bioconjugate of claim 10, wherein said nucleic acid or nucleic acid analogue is an oligonucleotide.

13 (Original): The bioconjugate of claim 10, wherein said nucleic acid is antisense DNA or RNA.

14 (Curently amended): The bioconjugate of claim 1, wherein said organocobalt complex is cobalamin, cobalamin lactone, cobalamin lactam, or a cobalamin derivative ~~or a cobalamine analogue~~, wherein said cobalamin derivative is (a) cobalamin in which the benzimidizaole ring is substituted with a halogen, hydroxy or a C₁₋₆ alkyl, (b) an anilide, ethylamide, monocarboxylic acid, dicarboxylic acid, tricarboxylic acid or propionamide derivative of cobalamin, or (c) cobalamin substituted with an amino, a nitro, a halogen, a sulfito, a C₂₋₆ alkylene or a C₂₋₆ alkyne.

15 (Currently amended): The bioconjugate of claim 1, wherein said organocobalt complex is a compound having the following formula:



wherein

~~the substituents may be included or omitted to modulate physical properties of the molecule, e.g., water solubility, stability of λ_{max} — the wavelength at which the complex absorbs~~ R is H, amino, C_{1-6} alcohol, or C_{1-6} carboxyl. W, W', X, X', Y, Y', Z and Z' are independently H, amino, C_{1-6} alcohol, C_{1-6} carboxyl, SO_3^- , CH_2OH , CO_2H , or nitro, or W and X together form a 4-6 member cyclic or heterocyclic ring, or W' and X' together form a 4-6 member cyclic or heterocyclic ring, or Y and Z together form a 4-6 member cyclic or heterocyclic aromatic ring or Y' and Z' together form a 4-6 member cyclic or heterocyclic aromatic ring.

16 (Currently amended): The bioconjugate of claim 15, which further comprises a targeting molecule covalently linked to one of said R, W, W', X, X', Y, Y', Z or Z', wherein said targeting molecule is selected from the group consisting of glucose, galactose, mannose, mannose 6-phosphate, transferrin, cobalamin, asialoglycoprotein, α -2-macroglobulins, insulin, a peptide growth factor, folic acid or derivatives, biotin or derivatives, YEE(GalNAcAH)₃ or derivatives, albumin,

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texaphyrin, metallotexaphyrin, a vitamin, a coenzyme, an antibody, an antibody fragment and a single-chain antibody variable region (scFv).

17 (Currently amended): The bioconjugate of claim 1, wherein said organocobalt complex is selected from the group consisting of organo(pyridine)bis(dimethylglyoximato)cobalt, a corrinoid or derivatives thereof and analogues thereof, wherein said derivative is (a) a corrinoid in which the benzimidazole ring is substituted with a halogen, hydroxy or a C₁₋₆ alkyl, (b) a corrinoid substituted with an amino, a nitro, a halogen, a sulfito, a C₂₋₆ alkylene or a C₂₋₆ alkyne, or (c) organo(pyridine)bis(dimethyl-glyoximato)cobalt substituted with an amino, a nitro, a halogen, a sulfito, a C₂₋₆ alkylene or a C₂₋₆ alkyne.

18 (Original): The bioconjugate of claim 1, wherein said organocobalt complex comprises a multiple unsaturated heterocyclic ring system bonded to a cobalt atom through 4-5 nitrogens and/or chalcogens which are part of said ring system.